DC3B, a diterpene obtained from *Caesalpinia pulcherrima* modulates stemness in NTERA-2 cancer stem-like cells

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Cancer is a multi-stage, heterogeneous disease characterized by the uncontrolled proliferation of cells, leading to tissue invasion and metastasis. A growing body of evidence attributes the malignant traits of cancer, including therapy resistance and recurrence, to a subpopulation of tumor cells known as cancer stem cells (CSCs). CSCs possess stem-like properties such as self-renewal, differentiation, sphere formation, and high tumorigenic potential, making them critical contributors to metastasis and treatment failure. The effectiveness of modern cancer therapy is often limited by high toxicity and failure to eliminate CSCs. Natural products have long served as a valuable source of anticancer compounds due to their ability to modulate multiple signaling pathways with relatively lower toxicity. *Caesalpinia pulcherrima*, a plant widely used in traditional medicine, contains several bioactive compounds, among which 6β-cinnamoyl-7α-hydroxyvouacapen-5α-ol (DC3B) has demonstrated significant antiproliferative activity across various cancer cell lines. Previous studies carried out at the Institute of Biochemistry, Molecular Biology and Biotechnology (IBMBB) revealed that DC3B inhibits the Wnt/β-catenin pathway, a critical regulator of CSC maintenance, by disrupting β-catenin/TCF interactions. The present study aimed to investigate the stemness-modulating potential of DC3B using NTERA-2 cancer stem-like cells as an *in vitro* CSC model. Treatment with DC3B significantly reduced colony formation ($p < 0.0001$) indicating suppressed self-renewal. Gene expression analysis further revealed that DC3B markedly downregulated the expression of key stemness-associated genes, *OCT4*, *SOX2*, and *NANOG*. A substantial reduction in AKT2 expression was also observed, suggesting an additional mechanism by which DC3B may impair CSC characteristics through modulation of the PI3K/AKT pathway. Collectively, these findings highlight the potential of DC3B as a CSC-targeting therapeutic agent.

Keywords: *CSCs, Natural products, Wnt/β-catenin, PI3K/AKT*